Citation:

Desch S, Schmidt J, Kobler D, Sonnabend M, Eitel I, Sareban M, Rahimi K, Schuler G, Thiele H. Effect of cocoa products on blood pressure: systematic review and meta-analysis. *Am J Hypertens*. 2010 Jan; 23(1): 97-103.

PubMed ID: 19910929

Study Design:

Meta-analysis or Systematic Review

Class:

M - <u>Click here</u> for explanation of classification scheme.

Research Design and Implementation Rating:



POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

Determine the effects of cocoa products on blood pressure (BP).

Inclusion Criteria:

- Investigated flavanol-rich cocoa products such as dark chocolate and cocoa beverages
- Random allocation to treatment and control group
- BP measurements at baseline and at a minimum of one more time point
- Because the meta-analysis was designed to study the effects of habitual intake of cocoa products on BP, studies included in the analysis were larger than single dose trials
- Minimum of two weeks of treatment duration was required.

Exclusion Criteria:

30 articles were excluded because:

- Study design did not meet pre-specified criteria, N=16
- Blood pressure reporting was insufficient to calculate effect size, N=one
- Publication or study did not examine blood pressure, N=three
- Single dose trial
- Studies with subjects on anti-hypertensive medication.

Description of Study Protocol:

Recruitment

Selection of studies included in systematic review:

- 332 articles were identified from literature search
- 40 potentially relevant articles were identified for full text review
- 10 RCTs were identified for review and meta-analysis.

Design

Systematic review and meta-analysis of 10 RCTs (six crossover design and four parallel design studies).

Blinding Used

Adequate blinding was not possible with dark vs. white chocolate studies (50% of studies). Investigators and end point assessment were blinded in most studies.

Intervention

The studies investigated flavanol-rich cocoa products such as dark chocolate and cocoa beverages. Flavanol intake varied across studies, between five and 17 mg of the flavanol sub-compound epicatechin.

Statistical Analysis

Meta-analysis.

Data Collection Summary:

Timing of Measurements

BP measurements at baseline and at a minimum of one more time point. Single dose trials were not included. Treatment duration ranged from two to 18 weeks.

Dependent Variables

Systolic and diastolic blood pressure (SBP and DBP).

Independent Variables

Dietary flavanol-rich cocoa intake: Flavanol intake varied widely across studies (e.g., between five to 17mg epicatechin).

Control Variables

- Position when subject BP was measured (sitting, standing or supine)
- No restriction made regarding age, gender, medication, baseline BGP, risk profile or comorbidities.

Description of Actual Data Sample:

- *Initial N*: Studies excluded with N<16
- Attrition (final N): Not specified; variable across the 10 RCTs included
- Age: No restriction on age
- Ethnicity: No restriction on ethnicity
- Other relevant demographics: Majority of studies used office BP to assess treatment effects

• *Anthropometrics:* Populations were either healthy normotensive adults or patients with pre-hypertension or stage 1 hypertension without anti-hypertensive medication.

Summary of Results:

Subgroups	Mean Difference in <u>Systolic</u> <u>BP</u>	Mean Difference in <u>Diastolic</u> <u>BP</u>
	(mmHg, 95% CI)	(mmHg, 95% CI)
Short-term trials	-5.2 (-6.9 to -3.5)	-2.9 (-4.6 to -1.2)
Medium-term trials	-3.0 (-3.5 to -2.5)	-1.8 (-2.5 to -1.0)
Lower baseline BP	-3.6 (-5.5 to -1.8)	-3.6 (-5.5 to -1.8)
Higher baseline BP	-5.3 (-7.9 to -2.6)	-5.3 (-7.9 to -2.6)
Lower flavanol content	-5.2 (-7.0 to -3.3)	-5.2 (-7.0 to -3.3)
Higher flavanol content	-4.0 (-5.6 to -2.3)	-4.0 (-5.6 to -2.3)

- Ten RCTs comprising 297 individuals were included in the analysis
- Populations studied were either normotensive or pre-hypertensive adults
- Treatment duration was two to eight weeks
- Mean BP change in the active treatment arms across all trials:
 - SBP: -4.5mmHg (95% CI: -5.9 to -3.2, P<0.001
 - DBP: -2.5mmHg (95% CI, -3.9 to -1.2, P<0.001)
- Meta analysis confirmed BP-lowering effect of flavanol-rich cocoa products in a larger set of trials than previously reported.

Author Conclusion:

The meta-analysis confirms the BP-lowering capacity of flavanol-rich cocoa products in a larger set of trials than previously reported.

Reviewer Comments:

- Authors note that there was significant statistical heterogeneity across studies
- Questions about the most appropriate dose and long-term side effects warrant further investigations before cocoa products can be recommended as a treatment option for hypertension.

Research Design and Implementation Criteria Checklist: Review Articles

Relevance Questions

1. Will the answer if true, have a direct bearing on the health of patients?

Yes

2.	Is the outcome or topic something that patients/clients/population groups would care about?	Yes
3.	Is the problem addressed in the review one that is relevant to nutrition or dietetics practice?	Yes
4.	Will the information, if true, require a change in practice?	Yes

Validity	Questions	
1.	Was the question for the review clearly focused and appropriate?	Yes
2.	Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search termsused described?	Yes
3.	Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased?	Yes
4.	Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible?	Yes
5.	Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined?	Yes
6.	Was the outcome of interest clearly indicated? Were other potential harms and benefits considered?	Yes
7.	Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described?	Yes
8.	Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed?	Yes
10.	Was bias due to the review's funding or sponsorship unlikely?	No